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14. ABSTRACT

This document describes the research tasks and educational activities in which the PI has been engaged during the second phase of this post-doctoral work. The PI has selected 300 dense breast masses for testing using an automated segmentation algorithm which combines region growing with cost function analysis. This method has been validated on all cases using overlap, accuracy, sensitivity, specificity, Dice Similarity Index, and kappa statistics by two expert radiologists. Two experiments have been performed, where the segmentation algorithm was tested on non-processed and background trend corrected images. The PI has attended oncology seminars, attended one scientific meeting, made two oral presentations, made one poster presentation, and her publication completed during the last phase of the award was selected for publication in a virtual biophysics journal during this time.

15. SUBJECT TERMS
Image segmentation, validation methods, CAD

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I. INTRODUCTION

Breast mass segmentation is arguably one of the most difficult tasks in the development of Computer-Aided Diagnostic (CAD_x) systems. The main objective of this research is to develop an image segmentation method for mammograms that contain dense tissue as well as for mammograms that contain dense/fatty tissue, while its second objective is to incorporate the segmentation method into a CAD_x system. Specifically, we intend to do the following: (1) To develop an automatic image segmentation scheme to separate clinically occult breast masses from surrounding tissue (2) To evaluate the method by comparing the ROIs with mammographers' drawings and (3) To separate masses from glandular tissues using the Multiple Circular Path Convolution Neural Network (MCPCNN) classifier.

II. BODY

During the past 12 months the PI has tested and validated an automatic image segmentation algorithm on a set of dense breast mass cases for both non-processed and background trend corrected images. This section of the annual summary provides a detailed description of the experiment and is divided into the following sections: (A) Segmentation Method – an overview of the automated image segmentation method (please see Appendix for detailed description of method) (B) Database and Experiments – description of masses used and experiments performed (C) Results – statistical and graphical results of the experiment (D) Discussion of Results and (E) Future Work.

A. Segmentation Method

The segmentation method used in this study evaluates the steepest changes within a probabilistic cost function in an effort to determine the computer segmented contour which is most closely correlated with expert radiologist manual traces. It segments breast masses by combining region growing with the analysis of a probability-based function [1]. Once a set of contours is grown using region growing the probability density functions inside and outside the contours are found. A function, which is the logarithm of these probability density functions, is then constructed. The function is then searched for possible steep change locations, i.e., sharp changes in the logarithm values, and the intensities corresponding to those locations are likely to produce contours which are highly correlated with expert traces. A detailed description of the method is provided in the manuscripts located in the appendix of this document [5-7].

B. Database and Experiments

Three-hundred forty-two cases have been selected from the University of South Florida's Digital Database for Screening Mammography (DDSM) [2], where 175 of these cases are cancerous masses and 167 of the cases are benign masses. The densities of all cases from the DDSM have been rated according to the American College of Radiology's (ACR) density scale, which ranges from 1-4. A breast containing a great deal of fatty tissue would receive a rating of 1 and a breast containing a great deal of dense tissue would receive a rating of 4. The current database contains 242 cases with a density rating of 3 and 100 cases with a density rating of 4. In the current experiment the cost likelihood function threshold values (TV_1 and TV_2) were set to 1800 and 1300, respectively. Approximately 300 of the cases were manually traced by two expert radiologists. All cases have been validated by both radiologists, where the validation measures are overlap, accuracy, sensitivity, specificity, Dice Similarity Index (DSI), and kappa statistics as described in the literature [3,4] and manuscripts [5-7]. Initially, the images were not pre-processed in order to preserve the true mass borders. In hopes of attaining higher validation statistical values, the PI applied the background trend correction technique to the entire dataset and ran a second segmentation experiment on the pre-processed images.

C. Results

1. Statistical Results

Tables 1-4 contain p-values for Analysis of Variance (ANOVA) tests, in which a set of intra-observer experiments were performed to determine the value of pre-processing on segmentation results. Specifically, the PI tested non-processed versus pre-processed datasets for all statistical measures, and both expert radiologists. A table entry containing "NS" implies that there were no statistically significant differences for a particular test. The computer produces the three traces which it feels are the closest contours to those traced by the expert radiologists, so the results shown in the table contain results for tests for all three groups. Further, the maximum values of statistical measures for a subset of cancer cases were found to find the proximity between the optimal region-growing trace as determined by the computer and the region-growing trace with the highest possible value for a particular measure.

Table 1 – ANOVA test P-values for Intra-observer Experiment:
Non-Processed vs. Pre-Processed Cancer Cases (Expert A)

	Overlap	**Accuracy**	**Sensitivity**	**Specificity**	**DSI**	**kappa**
Group 1 Trace	2.2×10^{-6}	NS	1.4×10^{-6}	3.4×10^{-3}	4.5×10^{-7}	1.4×10^{-3}
Group 2 Trace	4.0×10^{-4}	NS	1.3×10^{-5}	3.8×10^{-6}	9.4×10^{-5}	3.5×10^{-2}
Group 3 Trace	4.3×10^{-6}	NS	1.5×10^{-5}	2.7×10^{-4}	1.1×10^{-5}	2.8×10^{-2}

Table 2 – ANOVA test P-values for Intra-observer Experiment:
Non-Processed vs. Pre-Processed Benign Cases (Expert A)

	Overlap	**Accuracy**	**Sensitivity**	**Specificity**	**DSI**	**kappa**
Group 1 Trace	1.37×10^{-6}	NS	2.0×10^{-6}	NS	3.8×10^{-7}	2.9×10^{-5}
Group 2 Trace	2.2×10^{-3}	NS	1.6×10^{-5}	3.4×10^{-4}	4.9×10^{-4}	1.5×10^{-2}
Group 3 Trace	NS	NS	5.1×10^{-6}	4.6×10^{-5}	NS	NS

Table 3 – ANOVA test P-values for Intra-observer Experiment:
Non-Processed vs. Pre-Processed Cancer Cases (Expert B)

	Overlap	**Accuracy**	**Sensitivity**	**Specificity**	**DSI**	**kappa**
Group 1 Trace	3.5×10^{-5}	NS	2.0×10^{-6}	1.2×10^{-3}	1.1×10^{-5}	2.8×10^{-3}
Group 2 Trace	NS	NS	1.3×10^{-4}	6.4×10^{-8}	3.2×10^{-2}	NS
Group 3 Trace	NS	2.2×10^{-2}	7.0×10^{-4}	3.7×10^{-6}	NS	NS

Table 4 – ANOVA test P-values for Intra-observer Experiment:
Non-Processed vs. Pre-Processed Benign Cases (Expert B)

	Overlap	**Accuracy**	**Sensitivity**	**Specificity**	**DSI**	**kappa**
Group 1 Trace	9.8×10^{-7}	NS	1.7×10^{-6}	NS	2.3×10^{-7}	9.0×10^{-6}
Group 2 Trace	1.8×10^{-3}	NS	4.1×10^{-6}	1.3×10^{-4}	3.9×10^{-4}	6.8×10^{-3}
Group 3 Trace	NS	NS	3.7×10^{-7}	1.2×10^{-5}	NS	NS

Table 5 – Mean Statistical Values Non-Processed Cases: Expert A, Cancer Cases

	Overlap	**Accuracy**	**Sensitivity**	**Specificity**	**DSI**	**kappa**
Group 1 Trace	0.18	0.72	0.18	1.0	0.27	0.22
Group 2 Trace	0.34	0.76	0.37	0.997	0.47	0.39
Group 3 Trace	0.36	0.76	0.46	0.95	0.51	0.40

Table 6 – Mean Statistical Values Non-Processed Cases: Expert B, Cancer Cases

	Overlap	Accuracy	Sensitivity	Specificity	DSI	kappa
Group 1 Trace	0.36	0.81	0.39	0.97	0.50	0.42
Group 2 Trace	0.50	0.84	0.63	0.92	0.64	0.54
Group 3 Trace	0.47	0.81	0.70	0.86	0.62	0.50

Table 7 – Mean Statistical Values Pre-Processed Cases: Expert A, Cancer Cases

	Overlap	Accuracy	Sensitivity	Specificity	DSI	kappa
Group 1 Trace	0.17	0.72	0.18	1.0	0.27	0.22
Group 2 Trace	0.34	0.76	0.37	0.99	0.47	0.39
Group 3 Trace	0.36	0.75	0.46	0.95	0.51	0.40

Table 8 – Mean Statistical Values Pre-Processed Cases: Expert B, Cancer Cases

	Overlap	Accuracy	Sensitivity	Specificity	DSI	kappa
Group 1 Trace	0.25	0.83	0.26	1.0	0.37	0.33
Group 2 Trace	0.45	0.86	0.49	0.99	0.57	0.53
Group 3 Trace	0.43	0.84	0.59	0.94	0.58	0.51

Table 9 – Mean Values for Contour Yielding Maximum Value vs. Computer Choice Contours

	Mean Maximum Overlap Value	Mean Group 1 Overlap Value	Mean Group 2 Overlap Value	Mean Group 3 Overlap Value
Expert A	0.62	0.28	0.45	0.48
Expert B	0.60	0.47	0.50	0.36

2. Visual Results

Figures 1-4 show segmentation results for both the pre-processed and non-processed mass cases

.

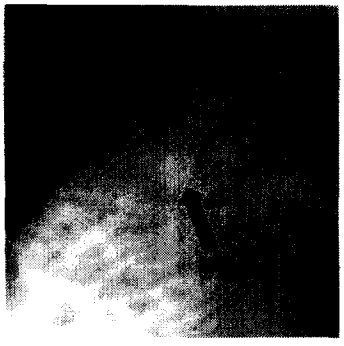

Figure 1a – Original Image
(Cancer Case, Density=3)

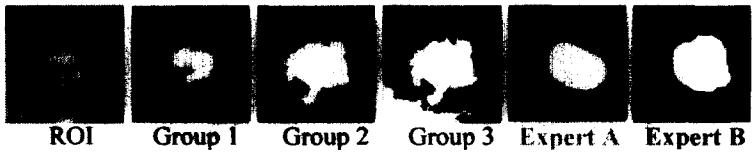

Figure 1b – Cropped original With Computer Results (Non-Processed Image)

Figure 1c – Cropped original With Computer Results (Pre-Processed Image)

Figure 1: Computer Segmentation Results for a Cancerous Mass

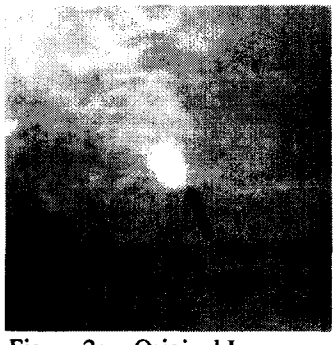

Figure 2a – Original Image
(Cancer Case, Density=3)

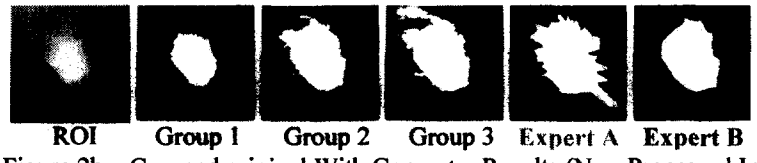

Figure 2b – Cropped original With Computer Results (Non-Processed Image)

Figure 2c – Cropped original With Computer Results (Pre-Processed Image)

Figure 2: Computer Segmentation Results for a Cancerous Mass

Figure 3a – Original Image
Benign Case, Density=3)

Figure 3b – Cropped original With Computer Results (Non-Processed Image)

Figure 3c – Cropped original With Computer Results (Pre-Processed Image)

Figure 3: Computer Segmentation Results for a Benign Mass

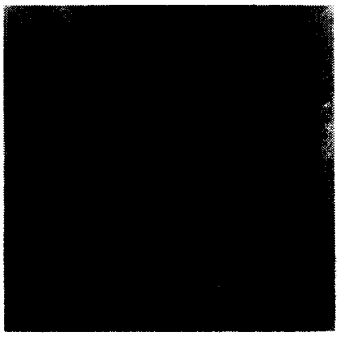

Figure 4a – Original Image
Benign Case, Density=3)

Figure 4b – Cropped original With Computer Results (Non-Processed Image)

Figure 4c – Cropped original With Computer Results (Pre-Processed Image)

Figure 4: Computer Segmentation Results for a Benign Mass

D. Discussion of Results

It has been observed that the segmentation algorithm produces better results using the non-processed images as inputs rather than using the pre-processed images as inputs, under the given set of parameters. As stated previously, the intensity corresponding to the location where the steep likelihood changes occur is likely to produce the contour that matches closely with the expert radiologist traces. The steep change location is determined by a set of threshold values determined by the user. The background trend correction process generally causes dark areas in the image to become darker, therefore, the contrast between the mass and background is higher for some cases. This, in turn creates more steep changes in the likelihood functions, which may have formerly been smooth. Therefore, the computer is likely to choose higher intensity values, consequently the contours will be small.

The ANOVA test results show that there were statistically significant differences between the non-processed and pre-processed images for both expert radiologists, for most statistics, where the mean values were higher for non-processed vs. pre-processed images for most statistics. These results imply that it may not be necessary to pre-process the images, but rather to use different parameters for the

automated selection process of finding optimal contours. Preliminary work has been done to determine how close the statistical values of the computer chosen contours are to those of the contours which obtain the greatest statistical values (see Table 9).

E. Future Work

During the next phase of this research the PI will complete the segmentation tasks and move to the diagnosis phase in which a CAD_x system will be used to diagnose the masses. A Linear Discriminant Analysis (LDA) algorithm will be used for feature selection and two types of neural networks will be used for classification. The PI will also compare the expert traces to one another in efforts to answer the questions around expert reliability and consistency.

III. KEY RESEARCH ACCOMPLISHMENTS

- Completed expert radiologist tracing of 300 masses
- Tested the efficacy of background trend correction upon segmentation improvement
- Added Dice Similarity Index (DSI) and kappa statistics as validation measures
- Validated masses using all validation measures
- Reviewed literature concerning inter-observer variability

IV. REPORTABLE OUTCOMES

Manuscripts:

1. L. Kinnard, S.-C. B. Lo, E. Makariou, T. Osicka, P. Wang, M.T. Freedman, M. Chouikha, "Steepest changes of a probability-based cost function for delineation of mammographic masses: A validation study," *J. of Medical Physics*, vol. 31, no. 10, 2004, pp. 2796-2810.
2. L. Kinnard, S.-C. B. Lo, E. Makariou, T. Osicka, P. Wang, M.T. Freedman, M. Chouikha, "Steepest changes of a probability-based cost function for delineation of mammographic masses: A validation study," *Virtual Journal of Biophysics*, Vol. 8, Issue 7, Oct. 1, 2004, http://www.vjbio.org/bio/ (selected across several medical and biophysics journals).
3. L. Kinnard, S.-C. B. Lo, E. Duckett, E. Makariou, M.T. Freedman, and M. Chouikha, "Mass Segmentation of Dense Breasts on Digitized Mammograms: Analysis of probability-based function," *Medical Imaging 2005: Image Processing, February, 2005, Proceedings of SPIE,* vol. 5747, pp. 1813-1823.

Poster Presentation:

1. L. Kinnard, S.-C. B. Lo, E. Duckett, E. Makariou, M.T. Freedman, and M. Chouikha, "Mass Segmentation of Dense Breasts on Digitized Mammograms: Analysis of probability-based function," *Medical Imaging 2005: Image Processing, February, 2005, Proceedings of SPIE,* vol. 5747, pp. 1813-1823.

Oral Presentations:

1. "The Post-Doctoral Experience: A Year in Review", *Preparing for the Postdoctoral Institute*, August, 2004, Howard University and The University of Texas at El Paso.
2. "Computer-Aided Diagnosis and Image Segmentation of Mammographic Masses", *Symposium on Translational Research for Cancer Detection, Diagnosis, Prevention, and Treatment*, The Howard University Cancer Center and the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, November, 2004.

Technical Development Activities:

- Attended meetings and one workshop of the Washington Academy of Biomedical Engineering (WABME)

- Attended cancer workshops conducted by the Howard University Cancer Center
- Attended SPIE Medical Imaging Meeting (February, 2005, San Diego, CA)

V. CONCLUSIONS

The background trend correction contrast enhancement method has the potential to produce reasonable segmentation results for the steepest change likelihood method under an appropriate set of steep change parameters. Further, the ANOVA statistical results reveal that there were statistically significant differences between the two processing methods for most statistics. In future work the PI would like to run similar experiments using different sets of parameters and using a set of consensus ground truth between two or more expert radiologists.

VI. REFERENCES

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6. L. Kinnard, S.-C. B. Lo, E. Makariou, T. Osicka, P. Wang, M.T. Freedman, M. Chouikha, "Steepest changes of a probability-based cost function for delineation of mammographic masses: A validation study," *J. of Medical Physics*, vol. 31, no. 10, 2004, pp. 2796-2810.
7. L. Kinnard, S.-C. B. Lo, E. Duckett, E. Makariou, M.T. Freedman, and M. Chouikha, "Mass Segmentation of Dense Breasts on Digitized Mammograms: Analysis of probability-based function," *Medical Imaging 2005: Image Processing, February, 2005, Proceedings of SPIE,* vol. 5747, pp. 1813-1823.